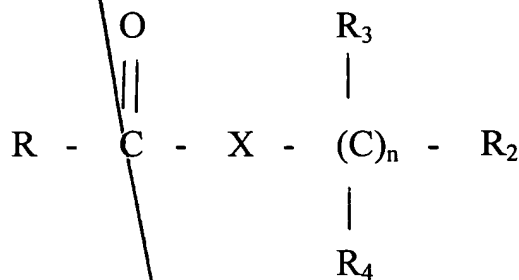


WHAT IS CLAIMED IS:

1. A method of ameliorating cough comprising the local administration to the upper respiratory airways of a subject in need of such treatment of a cannabinoid compound of formula I:



wherein X is N-R1 or O;

R is a saturated or unsaturated, chiral or achiral, cyclic or acyclic, substituted or unsubstituted hydrocarbonyl group with 11 to 29 carbon atoms;

R1, R3 and R4 are selected independently from hydrogen, alkyl (C1-4), alkenyl (C2-4), alkynyl (C2-4), cycloalkyl (C3-6), or hydroxyalkyl group with from 2 to 4 carbon atoms;

R2 is OH or O-CO-alkyl, where the alkyl group has from 1 to 4 carbon atoms;  
and

n is selected from 2 to 4.

2. The method of claim 1 wherein R comprises 1 to 6 oxygen or sulfur atoms.

4. The method of claim 3 wherein the heterocyclic ring structure is selected from the group consisting of an oxazolidinone ring and a morpholine ring.

$$\begin{array}{ccccccc} & \text{O} & \text{H} & \text{R}_3 & & & \\ & || & | & | & & & \\ \text{R} & - \text{C} & - \text{N} & - (\text{C})_n & - & \text{R}_2 & \\ & & & | & & & \\ & & & \text{R}_4 & & & \end{array}$$

R3 and R4 are selected independently from hydrogen, alkyl (C1-4), alkenyl (C2-4), alkynyl (C2-4), cycloalkyl (C3-6), or hydroxyalkyl group with from 2 to 4 carbon atoms;

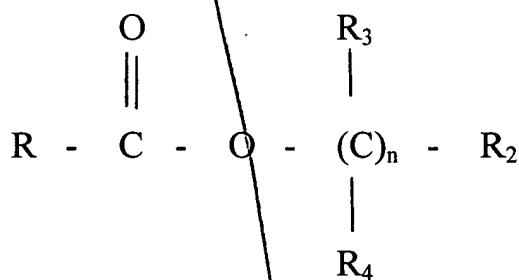
R2 is OH or O-CO-alkyl, where the alkyl group has from 1 to 4 carbon atoms;  
and

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6. The method of claim 5 wherein R comprises 1 to 3 oxygen or sulfur atoms.

7. The method of claim 5 wherein R<sub>2</sub> is OH and X is N-H, and wherein they combine to form a heterocyclic ring structure.

8. A method of ameliorating cough comprising the local administration to the upper respiratory airways of a subject in need of such treatment of a cannabinoid compound of formula III:



wherein R is a saturated or unsaturated, substituted or unsubstituted hydrocarbyl group with from 15 to 29 carbon atoms;

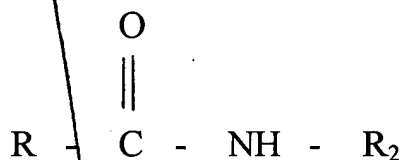
R<sub>3</sub> and R<sub>4</sub> are selected independently from hydrogen, alkyl (C1-4), alkenyl (C2-4), alkynyl (C2-4), cycloalkyl (C3-6), or hydroxyalkyl group with from 2 to 4 carbon atoms;

R<sub>2</sub> is OH or O-CO-alkyl, where the alkyl group has from 1 to 4 carbon atoms;  
and

n is selected from 2 to 4.

9. The method of claim 8 wherein R comprises 1 to 3 oxygen atoms.

10. A method of ameliorating cough comprising the local administration to the upper respiratory airways of a subject or the systemic administration to subject in need of such treatment of an inhibitor of endogenous cannabinoid inactivation of formula IV:

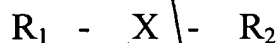


wherein R is a polyunsaturated, substituted or unsubstituted hydrocarbyl group with from 18 to 22 carbon atoms;

R<sub>2</sub> is selected independently from substituted or unsubstituted cycloalkyl (C<sub>3</sub>-6) group and substituted or unsubstituted phenyl group.

11. The method of claim 10 wherein the phenyl group is selected from the group consisting of p-hydroxyphenyl and p-hydroxy-o-methyl-phenyl.

12. A method of ameliorating cough comprising the local administration to the upper respiratory airways of a subject or the systemic administration to subject in need of such treatment of an inhibitor of endogenous cannabinoid inactivation of formula V:



wherein R<sub>1</sub> is a saturated or polyunsaturated, substituted or unsubstituted hydrocarbyl group with from 6 to 22 carbon atoms;

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X is  $\text{-C=O}$  or  $\text{SO}_2$ ; and

R2 is a halogen or a halogen-substituted methyl group.

13. The method of claim 1 wherein the cause of the cough can be persisting dry cough resulting from airway irritation and/or infection, angiotensin converting enzyme (ACE) inhibitors-induced cough, and cancer-induced cough.

14. The method of claim 10 wherein the method further comprises administration of a cannabinoid compound of formulae I, II, III, or any combination thereof.

15. The method of claim 11 wherein the method further comprises administration of a cannabinoid compound of formulae I, II, III, or any combination thereof.

16. A method of ameliorating cough comprising the local administration of a cannabinoid compound of formulae I, II, III, or any combination thereof, to the upper respiratory airways of patients in need of such treatment and whose vagal control of airway responsiveness is functional.

17. A method of selectively activating CB1 cannabinoid receptors of the upper respiratory airways, comprising locally administering to a subject in need of such treatment a cannabinoid compound of formulae I, II, III, or any combination thereof.

18. A method of ameliorating cough comprising the local administration to the upper respiratory airways of patients in need of such treatment, wherein the cannabinoid compound is sensitive to metabolic inactivation by transport or hydrolysis, causing clinically insignificant systemic side effects.

19. The method of claim 1 wherein a cannabinoid of formulae I is selected from the group consisting of arachidonylethanolamide (anandamide), (R)-(+)-arachidonyl-1'-hydroxy-2'-propylamide, cis-7,10,13,16-docosatetraenoylethanolamide, homo-delta-linoleylethanolamide, and N-propyl-arachidonylethanolamide.

20. The method of claim 10 wherein a cannabinoid inactivation inhibitor of formula IV is 4-(hydroxylphenyl)-arachidonylamide.

21. The method of claim 12 wherein a cannabinoid inactivation inhibitor of formula V is palmitylsulphonylfluoride or arachidonyltrifluoromethylketone.

22. A method of ameliorating cough comprising the local administration to the upper respiratory airways of a subject in need of such treatment of a pharmaceutical composition comprising a cannabinoid compound of formulae I, II, III, or any combination thereof.

23. The method of claim 22 wherein the method further comprises local or systemic administration of a pharmaceutical composition comprising a cannabinoid inactivation inhibitor of formulae IV, V, or any combination thereof.

24. The method of claim 23 wherein the pharmaceutical composition comprises compounds of formulae I, II, III, IV, V, or any combination thereof.

25. The method of claim 22, wherein the pharmaceutical composition is formulated for local delivery.

26. The method of claim 25 wherein the formulation for local delivery is by aerosol.

27. The method of claim 23 wherein the pharmaceutical composition is formulated for local delivery.

28. The method of claim 27 wherein the formulation for local delivery is by aerosol.

29. The method of claim 23 wherein the pharmaceutical composition is formulated for systemic delivery.

30. The method of claim 29 wherein the formulation for systemic delivery is by oral administration or intravenous administration.

31. A pharmaceutical composition comprising a locally acting cannabinoid of formulae I, II, III, or any combination thereof, wherein the cannabinoid ameliorates cough and produces, at most, clinically insignificant side effects.

32. The pharmaceutical composition of claim 31 further comprising a pharmaceutically acceptable excipient.

33. A pharmaceutical composition comprising a cannabinoid inactivation inhibitor of formulae IV, V, or any combination thereof, wherein the cannabinoid inactivation inhibitor ameliorates cough and produces, at most, clinically insignificant side effects.

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34. The pharmaceutical composition of claim 33 further comprising a pharmaceutically acceptable excipient.

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